

PROPERTIES AND PHARMACOLOGICAL APPLICATIONS OF SAPONINS

Deore S. L., Khadabadi S. S., K.P.Chittam, P. G. Bhujade,
T. P. Wane, Y. R. Nagpurkar, P. D. Chanekar, R. G. Jain

Government College of Pharmacy, Kathora Naka, Amravati - 444604. (M.S.), INDIA.
Email: khadabadi@yahoo.com, sharudeore_2@yahoo.com

Summary

Saponins are a diverse group of compounds widely distributed in the plant kingdom, which are characterized by their structure containing a triterpene or steroid aglycone and one or more sugar chains. They are believed to form the main constituents of many plant drugs and folk medicines, and are considered responsible for numerous pharmacological properties such as anticancer and anticholesterol activity. Hence it has led to the emergence of saponins as commercially significant compounds with expanding applications in food, cosmetics, and pharmaceutical sectors. This review provides an update on the sources, properties, and pharmacological applications of saponins.

KEYWORDS: Saponins, Triterpenes, Steroid, Sapogenins, Surfactants

Introduction

Saponins are glycosides containing one or more sugar chains (glycone part) on a triterpene or steroid aglycone skeleton hence classified into two groups steroidal and triterpenoidal saponins. Aglycone backbone of saponin is also called as a sapogenin. (Bruneton, 1995). Their structural diversity is reflected in their physicochemical and biological properties, which are exploited in a number of traditional and industrial applications. The nature of the aglycone and the functional groups on the aglycone backbone and number and nature of the sugars can vary greatly resulting in a very diverse group of compounds (Figure 1; Price et al., 1987; Hostettmann and Marston, 1995).

The presence of saponins has been reported in more than 100 families of plants, and in a few marine sources (Hostettmann and Marston, 1995). The saponin content of plant materials is affected by the plant species, genetic origin, and the part of the plant being examined, the environmental and agronomic factors associated with growth of the plant, and post-harvest treatments such as storage and processing (Fenwick et al., 1991). A single plant species may contain a complex mixture of saponins (e.g. soybean saponins, ginseng saponins (ginsenosides).

The name saponin is derived from the Latin word 'sapo', which means the plant that consists of frothing agent when diluted in aqueous solution (e.g. soapwort, soapberry, soapbark and soap root). These agents also cause haemolysis of red blood cells and thus they are highly toxic when injected directly into the blood stream. However saponins are relatively harmless when taken orally and some are found in most of our vegetables, beans and herbs. Toxicity is minimized during ingestion by low absorption and by hydrolysis. The well known sources of saponins are presented in Table 1.

Table 1: Commonly used saponins containing plant sources

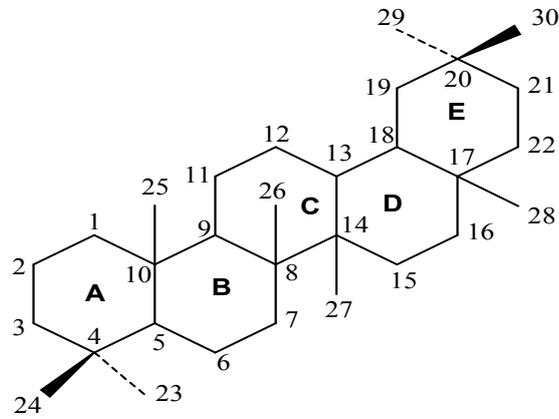
COMMON NAME	BIOLOGICAL SOURCE
Soybeans	<i>Glycine max</i>
Chickpeas	<i>Cicer arietinum</i>
Mungbeans	<i>Phaseolus aureus</i>
Peanuts	<i>Arachis hypogaea L</i>
Broad beans	<i>Vicia faba</i>
Kidney beans	<i>Phaseolus vulgaris</i>
Lentils	<i>Lens culinaris</i>
Leek	<i>Allium ampeloprasum var. porrum (L.)</i>
Garlic	<i>Allium sativum</i>
Asparagus	<i>Asparagus officinalis</i>
Spinach	<i>Spinacia oleracea</i>
Sugarbeet	<i>Beta vulgaris L</i>
Tea	<i>Camellia sinensis</i>
Yam	<i>Dioscorea villosa and other Dioscorea species</i>
Soap bark	<i>Quillaja saponaria</i>
Fenugreek	<i>Trigonella foenum-graceum</i>
Alfalfa	<i>Medicago sativa</i>
Chestnut horse	<i>Aesculus hippocastanum</i>
Licorice Glycyrrhiza	<i>Glycyrrhiza glabra</i>
Sarsaparilla	<i>Smilax regelii</i>
Soapwort Mojave	<i>Saponaria officinalis</i>
Yucca	<i>Yucca schidiger</i>
Gypsophila	<i>Gypsophila paniculata</i>
Ginseng	<i>Panax genus</i>

TRITERPENOID SAPONINS:

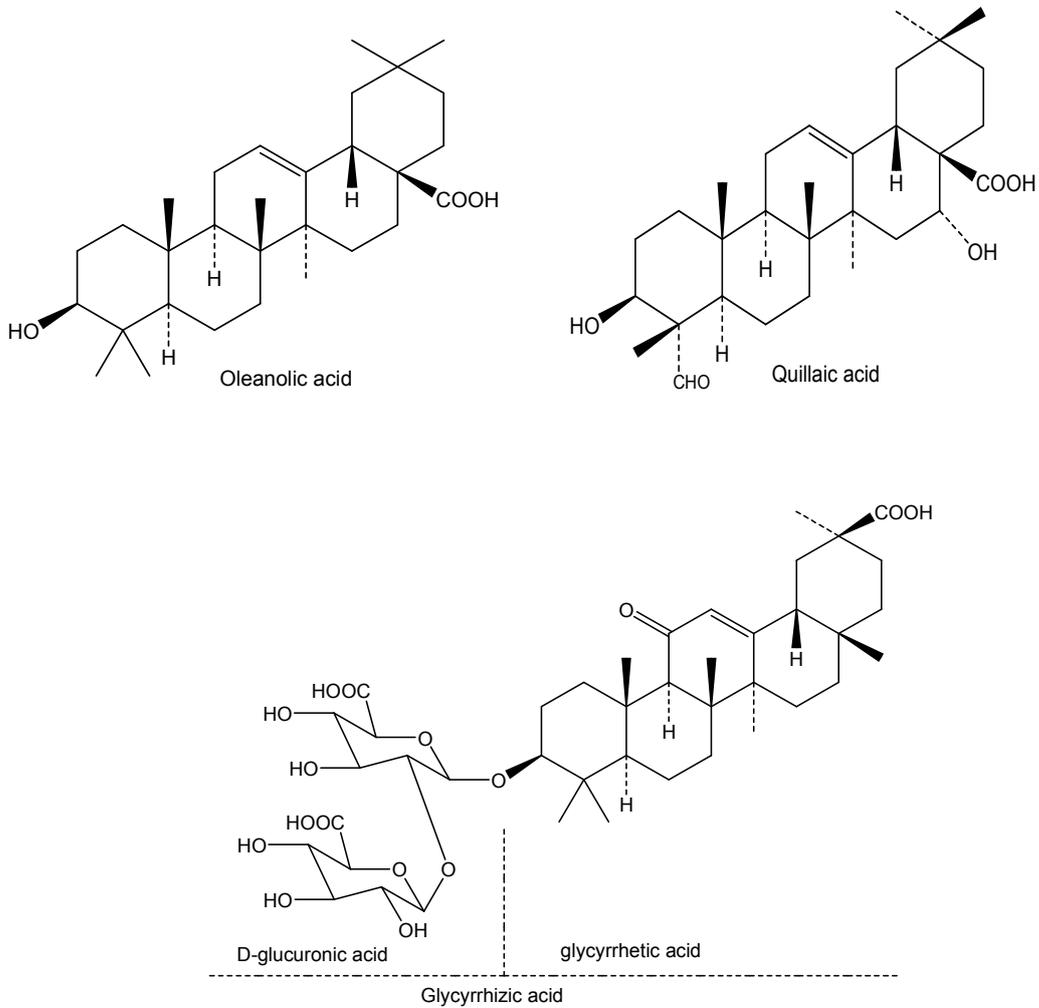
Triterpenoid saponins are rare in monocotyledons but abundant in many dicotyledons families (*Leguminosae*, *Araliaceae*, and *Caryophyllaceae*) (Sparg et al., 2004).

The pentacyclic triterpenoid skeleton exemplified by lupeol, α -amyrin and β -amyrin are usually found in triterpenoid saponin structures. Therapeutically important examples are mainly based on the β -amyrin subgroup mostly associated with carboxylic acid groups at positions C-23, C-28 and C-30 of aglycone moiety. Sometimes oxidized formyl (-CHO) or hydroxymethyl (-CH₂OH) groups may also be present. Sugar residues are usually attached to the 3-hydroxyl, with one to six monosaccharide units (e.g. glucose, galactose, rhamnose, arabinose, with uronic acid units (glucouronic acid and galactouronic acid). Figure 1 is showing basic backbone structures as well as examples of various commercially important triterpenoidal saponins.

Figure 1: TRITERPENOID SAPONINS



Pentacyclic triterpenoid skeleton



STEROIDAL SAPONINS:

The steroidal saponins have similar biological properties to the triterpenoid saponins but are less widely distributed in nature and are mainly found in monocotyledon families such as *Agavaceae*, *Dioscoreaceae* and *Liliaceae*, mainly the genera *Allium*, *Asparagus*, *Lilium*, *Agave*, *Yucca* and *Dioscorea* (Sparg et al., 2004).

Steroidal saponin are sterols in which the side chain of cholesterol has undergone some modification to produce further two different basic skeletons, one is C27 spirostane (largest group, six ring structure, eg. dioscin) and another one is C26 furostane (five ring structure). In case of spirostanols, sugar chain is attached at C-3 and spirokatal arrangement is linked at C-22. Structural variations of spirostanols are due to changes in stereochemistry at positions C-5 and C-25. Furostanol glycoside has the spirostanol like skeleton but with open side chain and sugar chain is attached not only to position C-3 but often also to C-26.

They are also further categorized according to the number of sugar chains in their structure as mono, di-, or tridesmosidic. Monodesmosidic saponins have a single sugar chain, normally attached at C-3. Bidesmosidic saponins have two sugar chains, often with one attached through an ether linkage at C-3 and one attached through an ester linkage at C-28 (triterpene saponins) or an ether linkage at C-26 (furostanol saponins). The most common monosaccharides include: D-glucose (Glc), D-galactose (Gal), D-glucuronic acid (GlcA), D-galacturonic acid (GalA), L-rhamnose (Rha), L-arabinose (Ara), D-xylose (Xyl), and D-fucose (Fuc).

Figure 2 is showing basic backbone structures as well as examples of various commercially important steroidal saponins.

STEROIDAL ALKALOIDS

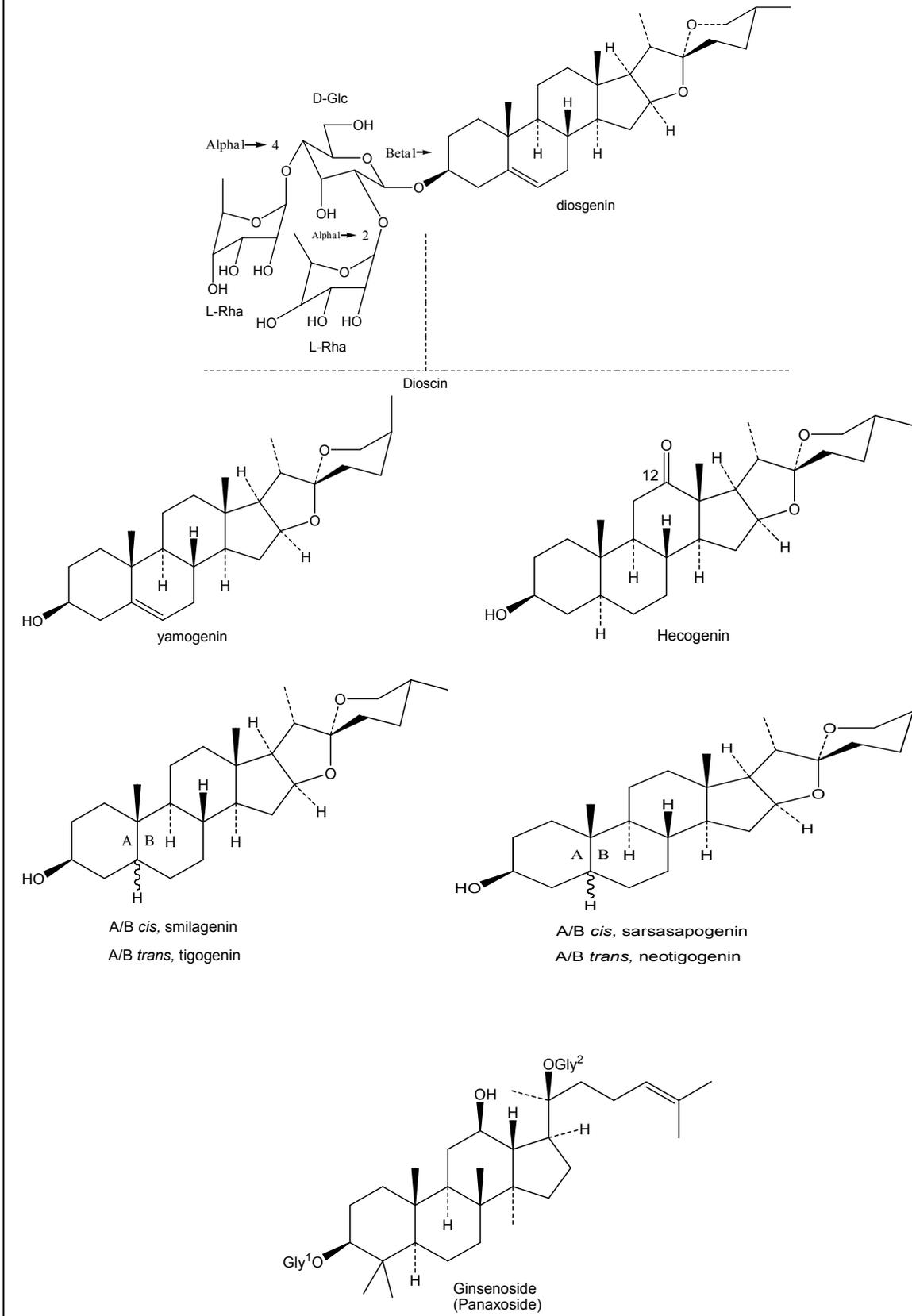
There is one more class which is a third group called steroidal amines and classified by others as steroidal alkaloids (Bruneton, 1995). These are actually nitrogen analogues of steroidal saponins and possess same properties such as surface activity and hemolytic activity but these compounds are highly toxic when injected (e.g. solasonine). Two important classes of these steroid alkaloids are the *Solanum* type and the *Veratrum* type.

Steroidal alkaloids also called as glycoalkaloids are most common in the families such as *Solanaceae*, *Apocynaceae*, and *Liliaceae*. Much of the recent work on this group of alkaloids was done by the group of Klaus Schreiber. Many of the plants that contain these alkaloids are of economic importance, e.g., *Solanum eleagnifolium*, *Solanum carolinense*, (horse nettle), *Solanum tuberosum* (potato), *Lycopersicon esculentum*, (tomato) all belonging to family *Solanaceae*, *Veratrum viride* and other species belonging to family *Liliaceae*, *Holarrhena antidysenterica*, family *Apocynaceae*.

There are 5 major structural types of steroidal alkaloids. These are the spirostanes (e.g. tomatidine and solasodine), solanidanes (e. g. verazine and etioline), 22, 26-epiminocholestanes (intermediates in the biosynthesis of spirostane, solanidine, a-epiminocyclohemiacetal, and 3-aminospirostane alkaloids), a-epiminocyclohemiacetals, and 3-aminospirostanes (e. g. tigogenin) (R. H. Manske, 1981).

The harmful and toxic saponins always referred as saptoxins which is fourth group of saponins.

Figure 2: STEROIDAL SAPONINS



PROPERTIES

The structural complexity of saponins results in a number of physical, chemical, and biological properties, only a few of which are common to all members of this diverse group. Due to the presence of a lipid-soluble aglycone and watersoluble sugar chain(s) in their structure (amphiphilic nature), saponins are surface active compounds with detergent, wetting, emulsifying, and foaming properties (Wang et al., 2005; Sarnthein-Graf and La Mesa, 2004; Mitra and Dungan, 1997; Ibanoglu and Ibanoglu, 2000). Micellar solubilization by saponins can be exploited for the development of micellar extraction processes or to affect the solubilization of ingredients in cosmetic, pharmaceutical or food formulations (Shirakawa et al., 1986).

Solubility of saponins is also affected by the properties of the solvent (as affected by temperature, composition, and pH). While water, alcohols (methanol, ethanol) and aqueous alcohols are the most common extraction solvents for saponins, solubility of some saponins in ether, chloroform, benzene, ethyl acetate, or glacial acetic acid has also been reported (Hostettmann and Marston, 1995).

While bitterness is the most common sensory attribute associated with saponins (Price et al., 1985), the occurrence of sweet saponins is also well known (Kennelly et al., 1996). For example, the sweetness of licorice is attributed to its main saponin, glycyrrhizic acid (Figure 1), which is 50 times sweeter than sugar (Muller and Morris, 1966).

The complex structure of saponins may undergo chemical transformations during storage or processing which in turn may modify their properties/activity. The glycosidic bond (between the sugar chain and the aglycone), and the interglycosidic bonds between the sugar residues can undergo hydrolysis in the presence of acids/alkali, due to hydrothermolysis (heating in presence of water) or enzymatic/microbial activity resulting in the formation of aglycones, prosapogenins, sugar residues or monosaccharides depending on the hydrolysis method and conditions (Hostettmann and Marston, 1995). Complete acid hydrolysis yields the constituent aglycone and monosaccharides, whereas under basic hydrolysis conditions, cleavage of

The solubility behavior of the parent aglycone can be markedly different than the saponin due to its lipophilic nature.

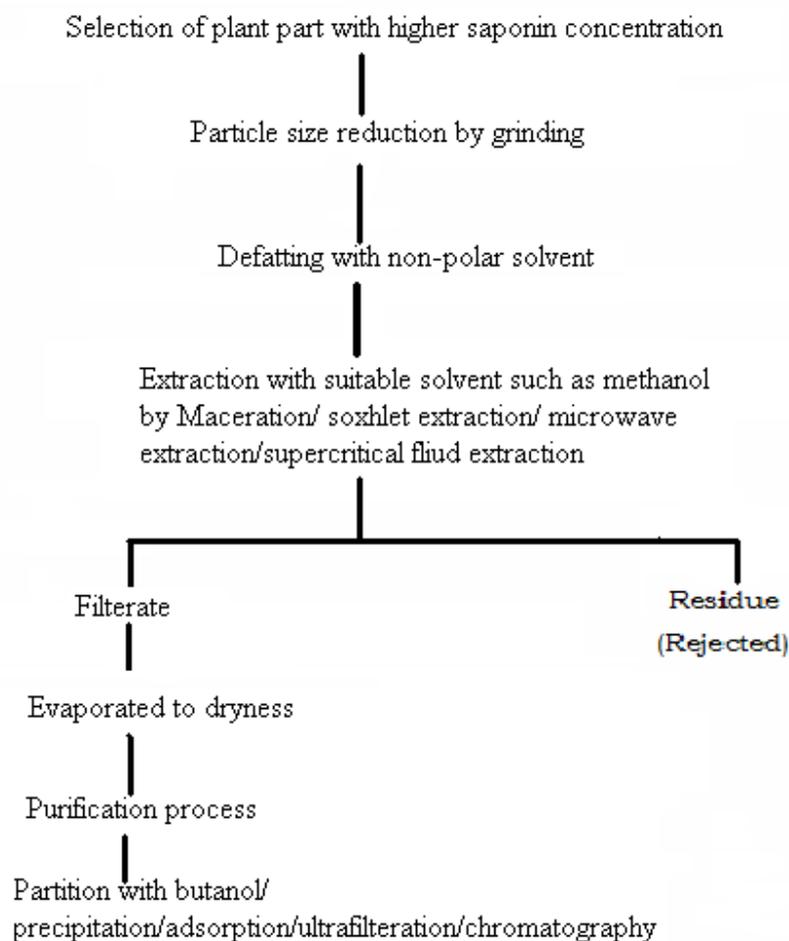
EXTRACTION AND PURIFICATION OF SAPONINS

The recognition of the commercial significance of saponins have prompted research on process development for the production of saponins on a commercial-scale from natural sources to recover saponins as separate fractions which requires a sequence of purification steps. As we have discussed in solubility aspect of saponin that water, alcohols (methanol, ethanol) and aqueous alcohols are the most common extraction solvents for saponins, solubility of some saponins in ether, chloroform, benzene, ethyl acetate, or glacial acetic acid has also been reported (Hostettmann and Marston, 1995). Aglycon part of saponins called sapogenins (obtained after separation of glycone-aglycone acid hydrolysis) is generally soluble in non-polar solvents.

Figure 3 is explaining detail process for extraction as well as purification of saponins.

Purification of the crude saponin extract usually requires a sequential approach. A first step for the preliminary purification of saponins after the extraction involves the partitioning of saponins between aqueous extracts and a water immiscible solvent such as *n*-butanol (Kitagawa, 1986). After removal of the solvent, the saponins can be separated by precipitation (Kitagawa, 1986; Nozomi *et al.*, 1986), adsorption (Giichi, 1987), ultrafiltration (Muir *et al.*, 2002), open-column chromatography on silica by gradient solvent system CHCl₃-MeOH-water (87:12:1-14:6:1), or by HPLC, flash chromatography, liquid chromatography (low, medium and high pressure), and countercurrent chromatography have been well established and widely used for analytical scale purification of saponins (Hostettmann and Marston, 1995).

Figure 3: Extraction and Purification of Saponins and Sapogenins



CHROMATOGRAPHIC DETERMINATION OF SAPONINS:

Chromatography is a powerful technique for determination of saponins (W. A. Oleszek, 2002).

TLC on normal and reversed phase is mostly used technique for separation and determination of large number of saponins. Silica gel is a preferred stationary phase while mobile phase consists of chloroform-methanol-water or butanol-acetic acid –water for saponins and benzene-acetone for aglycones. Visualisation sprayers include Anisaldehyde-Sulfuric acid, Vanillin-Sulphuric acid, Libermann-Burchard reagent, Carr-price reagent and phosphotungstic acid. TLC separated spots can be analysed either by colorimetric or densitometric method. In case of colorimetric method separated spots are scraped, extracted with alcohol and treated with a specific reagent such as Ehrlich or vanillin reagent and measured at wavelength 515-560 nm. In densitometric analysis on line coupling of a computer with a dual-wavelength flying –spot scanner and two dimensional analytical software are used to determine saponin identification and quantification.

Gas chromatography is another method of choice. But as saponins are polar and quite large molecules which are very difficult to volatilised. Hence first step in GC analysis of saponins is carefully monitored hydrolysis of intact saponin moiety to their aglycone moiety. Next step is to prepare acetyl, methyl or trimethylsilyl derivatives of this aglycone moiety to get analysed by GC.

The highly polar nature and high molecular mass of saponins, as well as their close structural similarities (isomers or epimers of the aglycone or sugar parts) can cause difficulties in TLC or CC, but the greater resolution of HPLC makes this the method of choice to deal with non-volatile highly polar intact saponin as well as aglycone. The separations are usually on normal (silica gel) and reversed phase (C8, C18) columns. C18 is most preferred but modified silica gel supports with NH₂ or DIOL are occasionally used. The main problem with HPLC analysis is detection since only few saponins (e.g. glycyrrhizic acid) have absorption maxima in UV range. The separation of majority of saponins has to be traced at lower UV wavelength ranging from 200 to 210 nm which further limits the selection of solvents. Since acetonitrile gives much lower absorption at lower wavelength hence acetonitrile-water system is better choice. Pre column derivatisation of saponins to attach chromophore is alternative method to low wavelength and Refractive index detector.

A rapid and convenient procedure of paper chromatography for the separation and identification of steroid saponins and their acetates has been described by E. Heftmann and A. L. Hayden, 1951. The method is based on partition chromatography in petroleum ether-toluene-alcohol by on water mixtures and subsequent detection of the compounds on the filter paper by spraying with either trichloroacetic acid or iodine.

BIOLOGICAL ACTIVITY

Saponins have been reported to possess a wide range of biological activities, which are Saponin-containing plants such as ginseng, yucca, horse chestnut, sarsaparilla, and licorice have been used in traditional medicine by various cultures for centuries for the prevention/ treatment of various ailments (Liu and Henkel, 2002; Hostettmann and Marston, 1995). Characterization of the medicinal plants and their extracts points to the role of saponins in conjunction with other bioactive components such as polyphenols in the observed health effects (Liu and Henkel, 2002; Alice et al., 1991). Table 2 is giving idea about diverse therapeutic effects of saponins.

Table 2: Various biological activities of saponins

Heamolytic activity		
Oda et al. (2000)	Escin saponins found in <i>Aesculus hippocastanum L.</i> (Hippocastanaceae) and jujuboside saponins from <i>Zizyphus jujuba Mill.</i> (Rhamnaceae)	Saponins with an acyl residue or oxide-ring moiety tended to show had strong haemolytic activity except for lablaboside d
Sindambiwe et al. (1998) Apers et al. (2001)	<i>Maesa lanceolata Forssk.</i> (Myrsinaceae)	Maesasaponins, substitution at position c-22 appears to be an essential structural feature for high haemolytic activity.
Voutquenne et al., (2003)	<i>Pometia ridleyi</i> (Sapindaceae).	Oleanolic saponin mixture showed higher haemolytic activity
Ahn et al. (1998)	<i>Bupleurum falcatum L.</i> (Apiaceae)	Saikosaponins-a, -d and -e were isolated and exhibited potent anti-cell adhesive activity and a strong haemolytic action.
Molluscicidal activity		
Sindambiwe et al., (1998) and Abdel-Gawad et al., (1999)	<i>Maesa lanceolata</i>	Six-oleanane-type triterpenoid maesasaponin mixture, with highly potent molluscicidal activity
Treyvaud et al., (2000)	<i>Phytolacca dodecandra L'Hér</i> and <i>Phytolacca icosandra L.</i> berries (Phytolaccaceae)	Monodesmosidic saponins of serjanic and spergulagenic acids with highly potent molluscicidal activity
Apers et al. (2001)	Leaves of <i>Maesa lanceolata</i>	Molluscicidal activity against biomphalaria glabrata snails.
Huang et al., (2003)	<i>Sapindus mukorossi Gaertn.</i> (Sapindaceae)	Triterpenoid hederagenin saponins had molluscicidal effects against the golden apple snail, pomacea canaliculata.

		Hederagenin saponins with three sugar moieties had higher molluscicidal activity than triterpene saponins with one sugar moiety.
Anti-inflammatory activity		
Just et al. (1998), Navarro et al., (2001)	<i>Bupleurum fruticosens L.</i> (Apiaceae),	Fruticesaponin b, a bidesmosidic saponin with an unbranched saccharide moiety shown highest anti-inflammatory activity of the all the saponins tested in the mouse oedema assays. Reducing the tpa-induced ear oedema
Sirtori, (2001)	<i>Aesculus hippocastanum L.</i> (Hippocastanaceae),	Aescin, a mixture of triterpenoid saponins has been shown to have anti-inflammatory, anti-oedematous and venotonic properties
Li et al. (2002)	Stem bark of <i>Kalopanax pictus</i> (Araliaceae).	Kalopanaxsaponin a and pictoside a were isolated triterpenoid saponin showed significant anti-inflammatory activity
Da Silva et al., (2002)	<i>Agave attenuata</i> Salm-Dyck (Agavaceae)	Steroidal saponin inhibited the increase in vascular permeability caused by acetic acid which is a typical model for the first stage inflammatory reaction.
Kwak et al., (2003)	Aerial parts of <i>Lonicera japonica</i> Thunb. (Caprifoliaceae)	Triterpenoid saponin loniceraside c showed anti-inflammatory activity when tested in vivo in the mouse ear oedema provoked by croton oil
Kim et al. (1998a)	<i>Panax ginseng</i> C.A. Mey., (Araliaceae)	Anti-inflammatory activity of these saponins is related to anticomplementary action through the classical inflammation pathway.
Antifungal activity		
Sindambiwe et al. (1998)	<i>Maesa lanceolata</i>	Mixture of maesasaponin inhibited the growth of epidermophyton floccosum, microides interdigitalis and trichophyton rubrum.

Ma et al., (1999).	<i>Panax notoginseng</i> (Burk.) (Araliaceae)	Inhibitory effect on aphanomyces cochlioides zoospore motility.
Li et al. (1999b)	<i>Colubrina retusa</i> L. (Rhamnaceae)	Jujubogenin saponins shown antifungal activity against candida albicans, cryptococcus neoformans and aspergillus fumigatus.
Miyakoshi et al., (2000)	<i>Yucca schidigera</i> (Agavaceae)	Steroidal saponins shown to exhibit effective growth-inhibitory activities against food-deteriorating yeasts, film-forming yeasts, and dermatophytic yeasts and fungi
Mshvildadze et al., (2000)	<i>Hedera colchica</i> (Araliaceae)	Monodesmosidic saponins shown antifungal and antiprotozoal activity. Saponins with hederagenin as their aglycone were more active than those without.
Woldemichael and Wink, (2001)	<i>Chenopodium quinoa</i> Willd. (Chenopodiaceae)	Triterpenoid saponins have been reported to have antifungal activity. Only the crude saponin mixture inhibited the growth of candida albicans.
Iorizzi et al., (2002)	Seeds of <i>Capsicum annuum</i> (Solanaceae)	Furostanol saponins showed stronger antiyeast activity than antifungal activity
Quiroga et al., (2001) and Escalante et al., (2002)	Different species of the genus <i>Phytolacca</i> (Phytolaccaceae)	Three olean-type triterpenoid saponins isolated from the berries of phytolacca tetramera hauman (phytolaccaceae) were tested for antifungal activity
De Lucca et al., (2002)	Fruits of <i>Capsicum frutescens</i> L. (Solanaceae)	Cay-1, a steroidal saponin isolated was shown to be a potent fungicide and antiyeast properties
Antimicrobial activity		
ElSohly et al., (1999)	<i>Colubrina retusa</i> L. (Rhamnaceae),	A new jujubogenin saponin isolated had antimycobacterial activity against mycobacterium intracellulare
Iorizzi et al. (2002)	Seeds of <i>Capsicum annuum</i> (Solanaceae).	Furostanol saponins along with seven known saponins from showed weak or no growth inhibition against both gram-positive and gram-negative bacteria.

Antiprotozoal activity		
Traore et al., (2000)	Aerial parts of <i>Glinus oppositifolius</i> L. (Molluginaceae)	Two new triterpenoid saponins, gminoside a and b, isolated were shown to have antiprotozoal activity against plasmodium falciparum
Delmas et al., (2000)	<i>Hedera helix</i> L. (Araliaceae)	Three saponins isolated from α - and β -hederin and hedeacolchiside a1, were shown to have antileishmanial activity on all the stages of development of the parasite leishmania infantum.
Anticancer/ cytotoxic activity		
Itabashi et al., (1999)	Leaves of <i>Furcraea foetida</i> (L.) Haw. (Agavaceae)	A novel steroidal saponin, furcreastatin, was screened for its selective cytotoxicity towards mutant p53-expressing mouse fibroblasts
Mimaki et al., (1998b); Mimaki et al., (1998c); Mimaki et al., (1999a); Mimaki et al., (1999c) and Mimaki et al., (2001b); Yokosuka et al., (2002b).		Many isolated steroidal saponins have been shown to be either cytostatic or cytotoxic to hl-60 human leukemia cell lines
Mimaki et al. (1998b)	<i>Ruscus aculeatus</i> L. (Liliaceae).	Saponins ruscogenin diglycoside (spirostanol saponin) and its corresponding 26-glycosyloxyfurostanol saponin showed cytostatic activity
Mimaki et al. (1999c)	Aerial parts of <i>Dracaena draco</i> L. (Dracaenaceae)	Only two of the tested saponins showed relatively potent cytostatic activity against the human promyelocytic leukemia hl-60 cells.
Xiao et al., (1999)	Root bark of <i>Aralia dasyphylla</i> Miq. (Araliaceae)	A novel triterpene saponin, showed significant cytotoxic activity against kb and hela-s3 cells
Lee et al. (1999)	<i>Panax ginseng</i> (Araliaceae)	Novel saponin metabolite (ih-901) which showed in vitro antitumor activity.
Yun (2003)	<i>Panax ginseng</i> (Araliaceae).	Activity of ginseng saponins are non-organ specific and that the anticarcinogenicity or human cancer preventative effect of panax ginseng is due

		to the ginsenoside saponins rg3, rg5 and rh2.
Mimaki et al. (1999a)	Roots of <i>Pulsatilla chinensis</i> (Ranunculaceae)	Triterpene saponins exhibited moderate cytotoxic activity
De Tommasi et al., (2000)	Aerial parts of <i>Trevesia palmata</i> . (Araliaceae)	Triterpenoid saponins cytotoxic against three continuous culture cell lines (j774, hek-293 and wehi-164)
Gaidi et al., (2000b)	Roots of <i>Acanthophyllum squarrosum</i> (Caryophyllaceae)	Higher concentrations of two new triterpenoid saponins were showed strong cytotoxicity in vitro for lymphocyte antiproliferation
Liu et al., (2000)	<i>Panax ginseng</i> (Araliaceae)	Saponins were shown to have antiproliferative effects on human prostate cancer cell lines
Qiu et al. (2000)	<i>Chlorophytum malayense</i> Ridl. (Liliaceae),	Saponin chloromaloside a which was found to be highly cytotoxic.
Zou et al., (2000)	Stem bark of <i>Albizia julibrissin</i> Durazz. (Leguminosae),	Julibroside j1 and julibroside j9, two diastereomeric saponins showed cytotoxic activity kb cancer cell lines
Fattorusso et al., (2000)	<i>Allium porrum</i> L. (Alliaceae)	Steroidal saponins were found to be cytotoxic to wehi 164 cells and j774 cells
Yui et al., (2001)	<i>Securidaca inappendiculata</i> Hassk. (Polygalaceae) roots	Securioside a and securioside b, cell death-inducing activity
Dong et al., (2001a) and Dong et al. (2001b)	<i>Dioscorea panthaica</i> Prain & Burkill (Dioscoreaceae)	Steroidal saponins showed to be cytotoxic to a375-s2, 1929 and hela cell lines.
Kuroda et al., (2001)	<i>Camassia leichtlinii</i> (Bak.) (Liliaceae)	Saponins have been shown to have cytotoxic activity against human oral squamous cell carcinoma (hsc-2) cells and normal human gingival fibroblasts
Park et al., (2001)	Stem bark of <i>Kalopanax pictus</i> (Araliaceae)	Hederagenin, -hederin, kalopanaxsaponin a (commonly known as α -hederin), kalopanaxsaponin i, and sapindoside c has potential antitumor applications
Barthomeuf et al., (2002)	<i>Hedera colchica</i> (Araliaceae)	Hederacolchiside a1, a new oleanolic acid monodesmoside demonstrated strong cytotoxicity activities on a number of cancer cells

Gaidi et al., (2002)	<i>Silene fortunei</i> Vis. (Caryophyllaceae)	Triterpene saponins were shown to increase the accumulation and cytotoxic activity of the anticancer agent cisplatin on human colon tumor cells
Yokosuka et al., (2002b)	Rhizomes of <i>Tacca chantrieri</i> André (Taccaceae)	Steroidal saponins were shown cytotoxic activity against hl-60 human promyelocytic leukemia cells.
Jayatilake et al., (2003)	Seedpods <i>Acacia victoriae</i> Benth. (Leguminosae),	Avicins d and g, showed potent cytotoxic activity against human t-cell leukemia (jurkat cells) in vitro.
Tezuka et al., (2000)	Fruits of <i>Acacia concinna</i> Wall. (Leguminosae),	Three new saponins, kinmoonosides a, b and c exhibited significant cytotoxicity against human ht-1080 fibrosarcoma cells
Marquina et al. (2001)		Mixtures of monodesmoside saponins have also been shown to be cytotoxic against p388 and colon cell lines.
Antiviral activity		
Kinjo et al., (2000)	Fabaceae family	Triterpenoid saponins from the have been reported to have anti-herpes virus activity
Apers et al., (2001)	Leaves of <i>Maesa lanceolata</i> Forssk. (Myrsinaceae)	Triterpenoid saponins no anti hiv activity
Gosse et al., (2002)	Fruits of <i>Tieghemella heckelii</i> (Sapotaceae)	Arganine c, a saponin strongly inhibited the entry of hiv
Sindambiwe et al., (1998)	<i>Maesa lanceolata</i> Forssk. (Myrsinaceae)	The maesasaponin mixture was reported to have both anti-herpes simplex virus type 1 (hsv-1) and poliovirus type 1 activity
Yang et al., (1999)	Seeds of <i>Aesculus chinensis</i> Bunge (Hippocastanaceae)	Escin saponins were caused hiv-1 protease inhibition
Adaptogenic activity		
Nocerino et al. (2000)	<i>Panax quinquefolium</i> L. and <i>Panax ginseng</i> (Araliaceae)	Ginseng saponins the aphrodisiac and adaptogenic properties
Kanzaki et al., 1998)	<i>Panax ginseng</i> (Araliaceae)	Wound healing
Kim et al. (1998b)	<i>Panax ginseng</i> (Araliaceae)	Antidopaminergic action of the saponins at the postsynaptic dopamine receptor.
Lee et al., (2000)	<i>Panax ginseng</i>	Saponins were also found to

	(Araliaceae)	have an effect on ethanol-induced amnesia
Yeilada and Takaishi, (1999)	Flowers of <i>Spartium junceum</i> L. (Leguminosae)	Oleanene-type saponin showed potent anti-ulcerogenic activity
Estrada et al., (2000)	<i>Polygala senega</i> L. (Polygalaceae)	Saponins had potential vaccine adjuvant activity, increasing specific immune responses in mice immunized with ovalbumin and hens immunized with rotavirus
Yoshikawa et al., (2003)	Roots and flower buds of <i>Panax notoginseng</i> (Burk.) (Araliaceae)	Triterpenoid saponins showed potent hepatoprotective effects on liver injury induced by -galactosamine and lipopolysaccharide
Parab and Mengi (2002)	<i>Acorus calamus</i> L. (Araceae)	Saponins tested for hyperlipidemic activity significantly decreased the serum cholesterol and triglyceride levels.
Manish Gautam et al (2004)	<i>Asparagus racemosus</i> (Willd.) (Liliaceae)	Potential immunoadjuvant that also offers direct therapeutic benefits
Mayank Thakur et al (2007)	<i>C. borivilianum</i> (Liliaceae)	Potent activity of ethanolic extract when compared to sapogenin fraction of <i>C. borivilianum</i> .
Hepatoprotective Activity		
Kinjo J. et.al (1998)	Roots of <i>Pueraria lobata</i>	All tested saponins showed hepatoprotective action
Hae-Ung Lee et.al (2005)	<i>Panax ginseng</i>	potent membrane stabilizing activity shoed by isolated saponin
Yoshikawa M. et.al (1997)	Roots of <i>Bupleurum scorzonerifolium</i> WILLD	Isolated saponins, bupleurosides III, VI, IX, and XIII, found to be exerting the hepatocytotoxic activity
Cardiovascular activity		
Hiromichi Matsuura (2001)	<i>Allium cepa</i>	Saponins account for the cholesterol-lowering effect of garlic
Glenda I Scott et.al (2001)	<i>Panax ginseng</i>	Demonstrated a direct depressant action of ginsenosides on cardiomyocyte contraction, which may be mediated in part through increased NO production.

Sagesaka-Mitane Y, (1996)	<i>Camellia sinensis var. sinensis</i>	Single administration of tea-leaf saponin at 50mg/kg, p.o. showed a long-lasting hypotensive effect and this effect was as potent as that of enalapril maleate at the dose of 3 mg/kg, p.o.
Antiarthritic activity		
Da Wei Li et.al (2003)	<i>Kalopanax pictus</i> bark	The ethyl acetate fraction exhibited antiarthritic activity, which resulted in the isolation of α -hederin, α -hederin methyl ester, and kalopanaxsaponin I.

COMMERCIAL APPLICATIONS

The diverse physicochemical and biological properties of saponins have been successfully exploited in a number of commercial applications in food, cosmetics, agricultural and pharmaceutical sectors. However from a commercial angle the steroidal saponins have been occupied a very important position in the therapeutic armamentarium which is evidence by examples such as raw material for synthesis of number of medicinally potent steroids (Vitamin D, sex hormones like testosterone, progesterone, oestradiol etc. cardiac glycosides (digoxin, digitoxin), corticosteroids (cortisone acetate, aldosterone), oral contraceptives (mestranol, norethisterone) and diuretic steroid (spirinolactone). The liquid soap of soap nut solution is effective and economical household cleaner and can be used for washing pet's fur and skin as this removes parasites leaving the pet clean, soft and protected from any further infestations. In India, it is used as a jewelry polish, by soaking jewelry into the liquid soap. Commercial saponins are mainly extracted from *Quillaja saponaria* and *Yucca schidigera*.

Conclusions

Saponins include a diverse group of compounds characterized by their structure containing a steroid or triterpenoid aglycone and one or more sugar chains. Their physicochemical and biological properties, few of which are common to all members of this diverse group, are increasingly being exploited in food, cosmetics and pharmaceutical sectors. Knowing the commercial potential due to their health benefits (especially anticancer and immunomodulator) requires new approach in discovering novel saponins with promising chemotherapeutic effects against dreadful diseases cancer and AIDS.

Table 3: COMMERCIAL APPLICATIONS OF SAPONINS

Food applications:	
Miyakoshi, M., 2000.	Yucca (Mohave yucca, <i>Yucca schidigera</i> Roezl Fla) and quillaja (quillaia, soap bark, <i>Quillaja saponaria</i> Mol Fla) are classified as food additives in the US
European Union	Quillaja extract is classified by the European Union as a foaming agent for use in water-based, flavored non-alcoholic drinks
Godwithus Co Ltd., 2005.	Soybean concentrates marketed as functional food ingredients and nutraceuticals (OrganicTechnologies, 2005), and aKorean ginseng extract called saponia
Kang et al., 1999, Bhaggan et al., 2001.	Oleanolic acid include as a flavoring agent to modify the aftertaste/taste of the artificial sweetener and in fat blends as crystal modifier
Micich et al., 1992; Richardson and Jimenez-Flores, 1994,	Complex Formation of saponins with cholesterol has been used for the removal of cholesterol from dairy products such as butter oil
Cosmetics Applications	
Yoo et al., 2003, Bonte et al., 1998, Bombardelli et al., 2001.	Delay the aging process of the skin and prevent acne
Indena, 2005; Olmstead, 2002; Brand and Brand, 2004.	As natural non-ionic surfactants, they find widespread use as emulsifying, foaming agents and detergents. shower gels, shampoos, foam baths, hair conditioners and lotions, liquid soaps, baby care products, mouth washes, and toothpastes
Pharmaceutical/Health Applications	
Diosgenin hecogenin from <i>Agave</i> Species	Steroid hormones and drugs synthesis of progesterone
CR Kensil, 2005	Immunological adjuvants in veterinary vaccine formulations
Ginseng Dammarane Sapogenins	The chemopreventive and chemotherapeutic activities
Betulinic acid derivatives Panacos, 2005	HIV drugs called Maturation Inhibitors inflammation
Forse and Chavali, 1997	Infection
Bombardelli and Gabetta, 2001	Alcoholism
Bombardelli and Gabetta, 2001	Pre- and post-menopausal symptoms
Yao et al., 2005	Cardiovascular and cerebrovascular diseases such as coronary
Hidvegi, 1994	Heart disease and hypertension
Ma et al., 2003	Prophylaxis and dementia
Satoshi et al., 2004	Ultraviolet damage including cataract, and carcinoma cutaneum
Kim et al., 2003a	Gastritis, gastric ulcer, and duodenal ulcer

References

1. Abdel-Gawad, M.M., El-Sayed, M.M. and Abdel-Hameed, E.S., (1999) Molluscicidal steroidal saponins and lipid content of *Agave decipiens*. *Fitoterapia* 70: 371–381.
2. Ahn, B.-Z., Yoon, Y.-D., Lee, Y.H., Kim, B.-H. and Sok, D.-E., (1998) Inhibitory effect of *bupleuri radix* saponins on adhesion of some solid tumor cells and relation to hemolytic action: Screening of 232 herbal drugs for anti-cell adhesion. *Planta Medica* 64: 220–224.
3. Alice, C.B., Vargas, V.M.F., Silva, G.A.A.B., de Siqueira, N.C.S., Schapoval, E.E.S., Gleye, J., Henriques, J.A.P., and Henriques, A.T. (1991) Screening of plants used in south Brazilian folk medicine. *J. Ethnopharmacol.*, 35:165

4. Apers, S., Varonikova, S., Sindambiwe, J.-B., Witvrouw, M., De Clercq, E., Vanden Berghe, D., Van Marck, E., Vlietinck, A. and Pieters, L., (2001) Antiviral, haemolytic and molluscicidal activities of triterpenoid saponins from *Maesa lanceolata*: establishment of structure–activity relationships. *Planta Medica* 67: 528–532.
5. Barthomeuf, C., Debiton, E., Mshvildadze, V., Kemertelidze, E. and Balansard, G., (2002) In vitro activity of hederacolchisid A₁ compared with other saponins from *Hedera colchica* against proliferation of human carcinoma and melanoma cells. *Planta Medica* 68:672–675.
6. Bhaggan, K., Cain, F.W., Pierce, J.H., Rogers, J.S., and Schmid, U. (2001) Fat blends with crystal modifiers. EP Patent 1,123,659 A1
7. Bombardelli, E., and Gabetta, B. (2001) Soya extract, process for its preparation and pharmaceutical composition. US Patent 6,280,777.
8. Bombardelli, E., Morazzoni, P., Cristoni, A., and Seghizzi, R. (2001) Pharmaceutical and cosmetic formulations with antimicrobial activity. US Patent Application 2001/0046525 A1.
9. Brand, H., and Brand, E. (2004) A weighty issue. *Soap, Perfumery & Cosmetics Asia*, March: 27–31.
10. Bruneton, J. (1995) *Pharmacognosy, Phytochemistry, Medicinal Plants*. Lavoisier Publishing, Paris, pp. 538–544 (ISBN 2-4730-0028-7).
11. CR Kensil, U Patel, M Lennick and D Marcianni Separation and characterization of saponins with adjuvant activity from *Quillaja saponaria* Molina cortex *The Journal of Immunology*, 146(2), 431-437.
12. da Silva, B.P., De Sousa, A.C., Silva, G.M., Mendes, T.P. and Parente, J.P., (2002) A new bioactive steroidal saponin from *Agave attenuata*. *Zeitschrift fur Naturforschung C* 57: 423–428.
13. Da Wei Li, Jin Ee Hyun, Choon Sik Jeong, Yeong Shik Kim, Eun Bang Lee (2003) Antiinflammatory activity of α -hederin methyl ester from the alkaline hydrolysate of the butanol fraction of *Kalopanax pictus* bark extract *Biological & pharmaceutical bulletin*, 26(4):429-433.
14. de Lucca, A., Bland, J.M., Vigo, C.B., Cushion, M., Selitrennikoff, C.P., Peter, J. and Walsh, T.J., (2002) CAY-1, a fungicidal saponin from *Capsicum* sp. fruit. *Medical Mycology* 40:131–137.
15. De Tommasi, N., Autore, G., Bellino, A., Pinto, A., Pizza, C., Sorrentino, R. and Venturella, P., (2000) Antiproliferative triterpene saponins from *Trevesia palmata*. *Journal of Natural Products* 63: 308–314.
16. Delmas, F., Di Giorgio, C., Elias, R., Gasquet, M., Azas, Mshvildadze, V., Dekanosidze, G., Kemertelidze, E., Timon-David, P.,(2000). Antileishmanial activity of three saponins isolated from ivy, α -hederin, β -hederin and hederacolchiside A₁, as compared to their action on mammalian cells cultured in vitro. *Planta Medica* 66: 343–347.
17. Dong, M., Feng, X.-Z., Wang, B.-X., Wu, L.-J. and Ikejima, T., (2001) Two novel furostanol saponins from the rhizomes of *Dioscorea panthaica* Prain et Burkill and their cytotoxic activity. *Tetrahedron* 57:501–506.
18. Dong, M., Feng, X.-Z., Wu, L.-J., Wang, B.-X. and Ikejima, T., (2001) Two new steroidal saponins from the rhizomes of *Dioscorea panthaica* and their cytotoxic activity. *Planta Medica* 67:853–857.

19. ElSohly, H.N., Danner, S., Li, X.-C., Nimrod, A.C. and Clark, A.M., (1999) New antimycobacterial saponin from *Colubrina retusa*. *Journal of Natural Products* 62:1341–1342.
20. Erich Heftmasn and Alma Levast Hayden (1951) Paper chromatography of steroid saponins and their acetates, *The journal of biochemistry*, 11: 47-55.
21. Escalante, A.M., Santecchia, C.B., López, S.N., Gattuso, M.A., Ravelo, A.G., Monache, F.D., Sierra, M.G. and Zacchino, S.A., (2002) Isolation of antifungal saponins from *Phytolacca tetramera*, an Argentinean species in critic risk. *Journal of Ethnopharmacology* 82:29–34.
22. Estrada, A., Katselis, G.S., Laarveld, B. and Barl, B., (2000) Isolation and evaluation of immunological adjuvant activities of saponins from *Polygala senega* L. *Comparative Immunology. Microbiology and Infectious Diseases* 23: 27–43.
23. Estrada, A., Li, B., and Laarveld, B. (1998) Adjuvant action of *Chenopodium quinoa* saponins on the induction of antibody responses to intragastric and intranasal administered antigens in mice. *Comp. Immunol. Microb.* 21:225– 236.
24. Fattorusso, E., Lanzotti, V., Tagliatalata-Scafati, O., Di Rosa, M. and Ianaro, A., (2000) Cytotoxic saponins from bulbs of *Allium porrum* L. *Journal of Agricultural and Food Chemistry* 48:3455–3462.
25. Fenwick, G. R., Price, K. R., Tsukamoto, C., and Okubo, K. (1991) Saponins. In: J.P.F. D’Mello, C.M. Duffus, and J.H. Duffus, Eds. *Toxic Substances in Crop Plants*. The Royal Society of Chemistry, Cambridge, :285–327.
26. Gaidi, G., Miyamoto, T., Laurens, V. and Lacaille-Dubois, M.-A., (2002) New acylated triterpene saponins from *Silene fortunei* that modulate lymphocyte proliferation. *Journal of Natural Products* 65:1568–1572.
27. Gaidi, G., Miyamoto, T., Rustaiyan, A., Laurens, V. and Lacaille-Dubois, M.-A., (2000) Two new biologically active triterpene saponins from *Acanthophyllum squarrosum*. *Journal of Natural Products* 63:1497–1502.
28. Giichi, H. (1987) Production of saponin containing no isoflavone from soybean embryo bud. JP Patent 62,005,917.
29. Glenda I Scott, Peter B Colligan, Bonnie H Ren, and Jun Ren (2001) Ginsenosides Rb1 and Re decrease cardiac contraction in adult rat ventricular myocytes: role of nitric oxide, *Br J Pharmacol.* November; 134(6): 1159–1165.
30. Gosse, B., Gnabre, J., Bates, R.B., Dicus, C.W., Nakkiew, P. and Huang, R.C.C., (2002) Antiviral saponins from *Tieghemella heckelii*. *Journal of Natural Products* 65:1942–1944.
31. Hae-Ung Lee, Eun-Ah Bae, Myung Joo Han, Nam-Jae Kim and Dong-Hyun Kim (2005) Hepatoprotective effect of ginsenoside Rb1 and compound K on tert-butyl hydroperoxide-induced liver injury *Liver International*, 25(5):1069 – 1073.
32. Hidvegi, M. (1994) Process for the preparation of a pharmaceutical composition selectively lowering the blood-lipid level. US 5,277,910.
33. Hiromichi Matsuura, (2001) Saponins in Garlic as Modifiers of the Risk of Cardiovascular Disease, *Journal of Nutrition*. 131:1000S-1005S.
34. Hostettmann, K., and Marston, A. (1995) Saponins. Cambridge University Press, Cambridge, New York.
35. Huang, H.-C., Liao, S.-C., Chang, F.-R., Kuo, Y.-H. and Wu, Y.-C., (2003) Molluscicidal saponins from *Sapindus mukorossi*, inhibitory agents of golden apple

- snails, Pomacea canaliculata. Journal of Agricultural and Food Chemistry 51: 4916–4919
36. Ibanoglu, E., and Ibanoglu, S. (2000) Foaming behavior of liquorice (Glycyrrhiza glabra) extract. Food Chem., 70:333–336.
 37. Indena. (2005) Horse chestnut saponins. <http://www.indena.com/pdf/cosmleaf.pdf>, accessed 24/8/2005.
 38. Iorizzi, M., Lanzotti, V., Ranalli, G., De Marino, S. and Zollo, F., (2002) Antimicrobial furostanol saponins from the seeds of Capsicum annum L. var. acuminatum. Journal of Agricultural and Food Chemistry 50:4310–4316.
 39. Itabashi, M., Segawa, K., Ikeda, Y., Kondo, S., Naganawa, H., Koyano, T. and Umezawa, K., (1999) A new bioactive steroidal saponin, furcreastatin, from the plant Furcraea foetida. Carbohydrate Research 323:57–62.
 40. Jayatilake, G.S., Freeberg, D.R., Liu, Z., Richheimer, S.L., Blake, M.E., Bailey, D.T., Haridas, V. and Gutterman, J.U., (2003) Isolation and structures of avicins D and G: in vitro tumor-inhibitory saponins derived from Acacia victoriae. Journal of Natural Products 66:779–783.
 41. Just, M.J., Recio, M.C., Giner, R.M., Cuéllar, M.J., M ñez, S., Bilia, A.R. and Ríos, J.-L., (1998) Anti-inflammatory activity of unusual lupane saponins from Bupleurum frutescens. Planta Medica 64:404–407.
 42. Kang, R. K. L., Zyzak, L. L., and Nakatsu, T. (1999) Flavored product additive and method for using same. US Patent 5, 948,460.
 43. Kanzaki, T., Morisaki, N., Shiina, R. and Saito, Y., (1998) Role of transforming growth factor- pathway in the mechanism of wound healing by saponin from Ginseng Radix rubra. British Journal of Pharmacology 125: 255–262
 44. Kennelly, E. J., Suttisri, R., and Kinghorn, A. D. (1996) Novel sweet-tasting saponins of the cycloartane, oleanane, secodammarane, and steroidal types. In: G.R.Waller, and K. Yamasaki, Eds., Saponins Used in Food and Agriculture. Plenum Press, New York, 13–24.
 45. Kim, D.-H., Bae, E.-A., Han, M.-J., Choo, M.-K., Park, E.-K., and Park, J.-H.(2003a) Novel use of the extract of processed panax genus plant and saponin compound isolated therefrom. US Patent Application 2003/0190377 A1.
 46. Kim, D.S., Oh, S.R., Lee, I.S., Jung, K.Yl., Park, J.D., Kim, S.I. and Lee, H-K., (1998) Anticomplementary activity of Ginseng saponins and their degradation products. Phytochemistry 47:397–399.
 47. Kim, H.-S., Jang, C.-G., Oh, K.-W., Oh, S., Rhee, H.-M., Rhee, G.-S., Seong, Y.-H. and Park, W.-K., (1998) Effects of ginseng total saponin on morphine-induced hyperactivity and conditioned place preference in mice. Journal of Ethnopharmacology 60:33–42.
 48. Kinjo J., Arao T., Udayama M. , Nohara T., (1998) Preventive effects of saponins from the Pueraria lobata root on in vitro immunological liver injury of rat primary hepatocyte cultures Planta medica, 64(5) :413-416.
 49. Kinjo, J., Yokomizo, K., Hirakawa, T., Shii, Y., Nohara, T. and Uyeda, M., (2000) Anti-herpes virus activity of fabaceous triterpenoidal saponins. Biological and Pharmaceutical Bulletin 23:887–889.
 50. Kitagawa, I. 1986. Method of isolating soyasaponins. US Patent 4,594,412.

51. Kuroda, M., Mimaki, Y., Hasegawa, F., Yokosuka, A., Sashida, Y. and Sakagami, H., (2001) Steroidal glycosides from the bulbs of *Camassia leichtlinii* and their cytotoxic activities. *Chemical and Pharmaceutical Bulletin* 49:726–731.
52. Kwak, W.J., Han, C.K., Chang, H.W., Kim, H.P., Kang, S.S. and Son, K.H., (2003) Loniceroside C, an antiinflammatory saponin from *Lonicera japonica*. *Chemical and Pharmaceutical Bulletin* 51:333–335.
53. Lee, S.-C., Moon, Y.-S. and You, K.-H., (2000) Effects of red ginseng saponins and nootropic drugs on impaired acquisition of ethanol-treated rats in passive avoidance performance. *Journal of Ethnopharmacology* 69:1–8.
54. Lee, S.-J., Sung, J.-H., Lee, S.-J., Moon, C.-K. and Lee, B.-H., (1999) Antitumor activity of a novel ginseng saponin metabolite in human pulmonary adenocarcinoma cells resistant to cisplatin. *Cancer Letters* 144:39–43.
55. Li, D.W., Lee, E.B., Kang, S.S., Hyun, J.E. and Whang, W.K., (2002) Activity-guided isolation of saponins from *Kalopanax pictus* with anti-inflammatory activity. *Chemical and Pharmaceutical Bulletin* 50:900–903.
56. Li, X.-C., ElSohly, H.N., Nimrod, A.C. and Clark, A.M., (1999) Antifungal jujubogenin saponins from *Colubrina retusa*. *Journal of Natural Products* 62:674–677
57. Liu, J., and Henkel, T. (2002) Traditional Chinese Medicine (TCM): Are polyphenols and saponins the key ingredients triggering biological activities? *Curr. Med. Chem.*, 9:1483–1485.
58. Liu, W.K., Xu, S.X. and Che, C.T., (2000) Anti-proliferative effect of ginseng saponins on human prostate cancer cell line. *Life Sciences* 67:1297–1306.
59. Ma, B., Dong, J., and Wang, B. (2003) Use of steroidal saponins for the prophylaxis or treatment of dementia, and novel steroidal saponin compounds. US Patent 6,593,301.
60. Ma, W.G., Mizutani, M., Malterud, K.E., Lu, S.L., Ducrey, B. and Tahara, S., (1999) Saponins from the roots of *Panax notoginseng*. *Phytochemistry* 52:1133–1139.
61. Manish Gautam, Sham Diwanay, Sunil Gairolac, Yojana Shinde, Pralhad Patki, and Bhushan Patwardhan, (2004) Immunoadjuvant potential of *Asparagus racemosus* aqueous extract in experimental system *Journal of Ethnopharmacology* Volume 91(2-3): 251-255.
62. Marquina, S., Maldonado, N., Garduño-Ramírez, M.L., Aranda, E., Villarreal, M.L., Navarro, V., Bye, R., Delgado, G. and Alvarez, L., (2001) Bioactive oleanolic acid saponins and other constituents from the roots of *Viguiera decurrens*. *Phytochemistry* 56:93–97.
63. Mayank Thakur, Shilpi Bhargava and V. K. (2007) Dixit Immunomodulatory Activity of *Chlorophytum borivillianum* Sant. F, *eCAM* 4(4):419-423.
64. Micich, T. J., Foglia, T. A., and Holsinger, V. H. (1992) Polymer-supported saponins: An approach to cholesterol removal from butteroil. *J. Agric. Food Chem.*, 40:1321–1325.
65. Mimaki, Y., Kuroda, M., Asano, T. and Sashi, Y., (1999) Triterpene saponins and lignans from the roots of *Pulsatilla chinensis* and their cytotoxic activity against HL-60 cells. *Journal of Natural Products* 62:1279–1283.
66. Mimaki, Y., Kuroda, M., Ide, A., Kameyama, A., Yokosuka, A. and Sashida, Y., (1999) Steroidal saponins from the aerial parts of *Dracaena draco* and their cytostatic activity on HL-60 cells. *Phytochemistry* 50:805–813.

67. Mimaki, Y., Kuroda, M., Kameyama, A., Yokosuka, A. and Sashida, Y., (1998) Steroidal saponins from the underground parts of *Ruscus aculeatus* and their cytostatic activity on HL-60 cells. *Phytochemistry* 48:485–493.
68. Mimaki, Y., Kuroda, M., Kameyama, A., Yokosuka, A. and Sashida, Y., (1998) Steroidal saponins from the rhizomes of *Hosta sieboldii* and their cytostatic activity on HL-60 cells. *Phytochemistry* 48:1361–1369.
69. Mimaki, Y., Watanabe, K., Ando, Y., Sakuma, C., Sashida, Y., Furuya, S. and Sakagami, H., (2001) Flavonol glycosides and steroidal saponins from the leaves of *Cestrum nocturnum* and their cytotoxicity. *Journal of Natural Products* 64:17–22.
70. Miyakoshi, M., Tamura, Y., Masuda, H., Mizutani, K., Tanaka, O., Ikeda, T., Ohtani, K., Kasai, R. and Yamasaki, K., (2000) Antiyeast steroidal saponins from *Yucca schidigera* (Mohave yucca), a new anti-food-deteriorating agent. *Journal of Natural Products* 63:332–338.
71. Mshvildadze, V., Favel, A., Delmas, F., Elias, R., Faure, R., Decanosidze, G., Kemertelidze, E. and Balansard, G., (2000) Antifungal and antiprotozoal activities of saponins from *Hedera colchica*. *Pharmazie* 55:325–326.
72. Muir, A. D., Paton, D., Ballantyne, K., and Aubin, A. A. (2002) Process for recovery and purification of saponins and sapogenins from quinoa (*Chenopodium quinoa*). US Patent 6,355,249.
73. Muller, R.E., and Morris, R.J. Jr. (1966) Sucrose-ammoniated glycyrrhizin sweetening agent. US Patent 3,282,706.
74. Navarro, P., Giner, R.M., Recio, M.C., Máñez, S., Cerdá-Nicols, M. and Ríos, J.-L., (2001) In vivo anti-inflammatory activity of saponins from *Bupleurum rotundifolium*. *Life Sciences* 68:1199–1206.
75. Nocerino, E., Amato, M. and Izzo, A.A., (2000) The aphrodisiac and adaptogenic properties of ginseng. *Fitoterapia* 71: S1–S5
76. Nozomi, O., Haruo, S., Shisai, R., Fuku, S., Hikari, J., Toshi, H., and Bunshi, K. (1986) Saikosaponin. JP Patent 61,282,395.
77. Oda, K., Matsuda, H., Murakami, T., Katayama, S., Ohgitani, T. and Yoshikawa, M., (2000) Adjuvant and haemolytic activities of 47 saponins derived from medicinal and food plants. *Biological Chemistry* 381:67–74.
78. Olmstead, M. J. (2002) Organic toothpaste containing saponin. US Patent 6,485,711 B1.
79. Panacos. (2005) A new generation of anti-infective drugs. <http://www.panacos.com/product2.htm>, accessed 11/10/2005.
80. Parab, R.S. and Mengi, S.A., (2002) Hypolipidemic activity of *Acorus calamus* L. in rats. *Fitoterapia* 73:451–455.
81. Park, H.-J., Kwon, S.-H., Lee, J.-H., Lee, K.-H., Miyamoto, K.I. and Lee, K.-T., (2001) Kalopanaxsaponin A is a basic saponin structure for the anti-tumor activity of hederagenin monodesmosides. *Planta Medica* 67:118–121.
82. Price, K. R., Griffiths, N. M., Curl, C. R., and Fenwick, G. R. (1985) Undesirable sensory properties of the dried pea (*Pisum sativum*). The role of saponins. *Food Chem.*, 17:105–115.
83. Price, K. R., Johnson, I. T., and Fenwick, G. R. (1987) The chemistry and biological significance of saponins in foods and feeding stuffs. *CRC Crit. Rev. Food Sci.*, 26:27–135.

84. Qiu, S.-X., Li, X.-C., Xiong, Y., Dong, Y., Chai, H., Farnsworth, N.R., Pezzuto, J.M. and Fong, H.H.S., (2000) Isolation and characterization of cytotoxic saponin chloromaloside A from *Chlorophytum malayense*. *Planta Medica* 66P:587–590.
85. Quiroga, E.N., Sampietro, A.R. and Vattuone, M.A., (2001) Screening antifungal activities of selected medicinal plants. *Journal of Ethnopharmacology* 74:89–96.
86. R. H. Manske, Geoffrey A. Cordell, R. G. A. Rodrigo, H.L. Holmes, Arnold Brossi *Alkaloids Chemistry and Physiology: The alkaloid chemistry and physiology* Published by Academic Press, 1981.
87. Richardson, T., and Jimenez-Flores, R. (1994) Process to remove cholesterol from dairy products. US Patent 5,326,579.
88. Sagesaka-Mitane Y, Sugiura T, Miwa Y, Yamaguchi K, Kyuki K. (1996) Effect of tea-leaf saponin on blood pressure of spontaneously hypertensive rats, *Yakugaku Zasshi*. 116(5):388-95.
89. Sarnthein-Graf, C., and La Mesa, C. (2004) Association of saponins in water and water-gelatine mixtures. *Thermochim. Acta*, 418:79–84.
90. Satoshi, M., Erihi, O., and Satariyo, G. (2004) Composition for preventing or ameliorating ultraviolet damage. JP Patent 2,004,131,431.
91. Shirakawa, Y., Itoh, M., Koyama, K., and Minowa, Y. (1986) Aqueous preparation containing vitamin E and saponins. US Patent 4,568,667.
92. Sindambiwe, J.B., Calomme, M., Geerts, S., Pieters, L., Vlietinck, A.J. and Vanden Berghe, D.A., (1998) Evaluation of biological activities of triterpenoid saponins from *Maesa lanceolata*. *Journal of Natural Products* 61:585–590.
93. Sirtori, C.R., (2001) Aescin: Pharmacology, pharmacokinetics and therapeutic profile. *Pharmacological Research* 44:183–193.
94. Sparg, S.G., Light, M.E., and van Staden, J. (2004) Biological activities and distribution of plant saponins. *J. Ethnopharmacol.*, 94:219–243.
95. Tezuka, Y., Honda, K., Banskota, A.J., Thet, M.M. and Kadota, S., (2000) Kinmoonosides A–C, three new cytotoxic saponins from the fruits of *Acacia concinna*, a medicinal plant collected in Myanmar. *Journal of Natural Products* 63:1658–1664.
96. Traore, F., Faure, R., Olivier, E., Gasquet, M., Azas, N., Debrauwer, L., Keita, A., Timon-David, P. and Balansard, G., (2000) Structure and antiprotozoal activity of triterpenoid saponins from *Glinus oppositifolius*. *Planta Medica* 66:368–371.
97. Treyvaud, V., Marston, A., Dyatmiko, W. and Hostettmann, K., (2000) Molluscicidal saponins from *Phytolacca icosandra*. *Phytochemistry* 55:603–609.
98. Voutquenne, L., Guinot, P., Thoison, O., Sevenet, T. and Lavaud, C., (2003) Oleanolic glycosides from *Pometia ridleyi*. *Phytochemistry* 64:781–789.
99. W A Oleszek Chromatographic determination of plant saponins *Journal of chromatography. A*. 08/2002; 967(1):147-62.
100. Wang, Z.-W., Gu, M.-Y., and Li, G.-Z. (2005) Surface properties of gleditsia saponin and synergisms of its binary system. *J. Disper. Sci. Technol.*, 26:341–347.
101. Woldemichael, G.M. and Wink, M., (2001) Identification and biological activities of triterpenoid saponins from *Chenopodium quinoa*. *Journal of Agricultural and Food Chemistry* 49:2327–2332.

102. Xiao, K., Yi, Y.-H., Wang, Z.-Z., Tang, H.-F., Li, Y.-Q. and Lin, H.-W., (1999) A cytotoxic triterpene saponin from the root bark of *Aralia dasyphylla*. *Journal of Natural Products* 62:1030–1032.
103. Yang, X.-W., Zhao, J., Cui, Y.-X., Liu, X.-H., Ma, C.-M., Hattori, M. and Zhang, L.-H., (1999) Anti-HIV-1 protease triterpenoid saponins from the seeds of *Aesculus chinensis*. *Journal of Natural Products* 62:1510–1513
104. Yao X., Li, L., and Wang N. (2005) New use of saponin compound for treating cardiovascular disease. CN Patent 1,562,064.
105. Yeda, E. and Takaishi, Y., (1999) A saponin with anti-ulcerogenic effect from the flowers of *Spartium junceum*. *Phytochemistry* 51:903–908.
106. Yokosuka, A., Mimaki, Y. and Sashida, Y., (2002) Spirostanol saponins from the rhizomes of *Tacca chantrieri* and their cytotoxic activity. *Phytochemistry* 61:73–78.
107. Yokosuka, A., Mimaki, Y. and Sashida, Y., (2002) Spirostanol saponins from the rhizomes of *Tacca chantrieri* and their cytotoxic activity. *Phytochemistry* 61:73–78.
108. Yoo, B.H., Kang, B.Y., Yeom, M.H., Sung, D.S., Han, S.H., Kim, H.K., and Ju, H.K. (2003) Nanoemulsion comprising metabolites of ginseng saponin as an active component and a method for preparing the same, and a skin care composition for anti-aging containing the same. US Patent Application 2003/0175315 A1.
109. Yoshikawa M., Matsuda H, Murakami T., Ninomiya K., Inadzuki M., (1997) New hepatoprotective saponins, bupleurosides III, VI, IX, and XIII, from Chinese *Bupleuri Radix*: Structure-requirements for the cytoprotective activity in primary cultured rat hepatocytes, *Bioorganic & medicinal chemistry letters*, 7(17):2193-2198.
110. Yoshikawa, M., Morikawa, T., Kashima, Y., Ninomiya, K. and Matsuda, H., (2003) Structures of new dammarane-type triterpene saponins from the flower buds of *Panax notoginseng* and hepatoprotective effects of principal ginseng saponins. *Journal of Natural Products* 66, 922–927
111. Yui, S., Ubukata, K., Hodono, K., Kitahara, M., Mimaki, Y., Kuroda, M., Sashida, Y. and Yamazaki, M., (2001) Macrophage-oriented cytotoxic activity of novel triterpene saponins extracted from roots of *Securidaca inappendiculata*. *International Immunopharmacology* 1:1989–2000.
112. Yun, T.-K., (2003) Experimental and epidemiological evidence on non-organ specific cancer preventive effect of Korean ginseng and identification of active compounds. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis* 523/524:63–74.
113. Zou, K., Zhao, Y., Tu, G., Cui, J., Jia, Z. and Zhang, R., (2000) Two diastereomeric saponins with cytotoxic activity from *Albizia julibrissin*. *Carbohydrate Research* 324:182–188.